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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,808	03/15/2000	Athanasius A Anagnostou	5218-39C	9764

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EXAMINER	
YAEN, CHRISTOPHER H	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/525,808	ANAGNOSTOU ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17,19,20,22,31-33 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,17,19,20,22,31-33 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibit A*.

DETAILED ACTION

RE: Anagnostou et al
Priority Date: 11 September 1996

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/30/2004 has been entered.

2. Claims 1-15, 18,21,23-30, and 34-39 are canceled without prejudice or disclaimer.

3. Claims 16-17,19-20,22,31-33, and 40 are pending and examined on the merits.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained - 35 USC § 102

5. The rejection of claims 16, 31-33 and now newly rejected claims 17,19,20 under 35 USC § 102(b) as being anticipated by Silvestris *et al* (Ann Hematol. 1995 Jun; 70(6):313-318, previously cited) is maintained for the reasons of record. Applicant does not provide any arguments to rebut the rejections, but instead has amended the claims to limit the mechanism of injury to the endothelial cells. Applicant's amendments have

been carefully considered but are not deemed persuasive to overcome the rejection of record. Silvestris *et al* teach a method of administrating erythropoietin (epo) to patients that have been treated with chemotherapeutics (see page 314). It is well known and established in the art (as evidenced by de Vos *et al* (Cancer Treat Rev. 2004 Oct;30(6):495-513) that the administration of chemotherapeutics to subjects cause vascular cytotoxicity/damage which include symptoms such as myocardial ischemia (a form of heart disease), vasculitis/inflammation of the blood vessel (see page 498), and in some cases physical disruption, such as cellular detachment (see page 500). Because the specification does not specifically define or limit the scope of the term "mechanical" damage or the types of heart disease encompassed, for the purposes of this rejection, the terms have been interpreted as any means of physical damage/disruption and any type of heart related ailment, respectively. Thus it is clear that the administration of a chemotherapeutic regimen as taught by Silvestris *et al* caused endothelial damage mediated by mechanical damage, inflammation, and heart disease and therefore, the administration of epo to this population would also inherently treat endothelial injury as claimed. Moreover, because the mechanism of action is not patentable subject matter and because it appears that the method steps and product administered are identical, in the absence of evidence to the contrary and because the office does not have the facilities to determine otherwise, the method taught by Silvestris *et al* would also treat endothelial cell injury as claimed. In the absence of evidence to the contrary, the method of Silvestris *et al* would also inherently reduce the

suppression of endothelial cells growth and increase the number of endothelial cells growth as claimed.

Therefore, the rejection of the claims under 35 USC 102(b) as being anticipated by Silvestris *et al* is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 16,22,31-33, and 40 and now newly rejected claims 17, and 19-20 under 35 USC § 102(b) as being anticipated by JP 02 096535 to Chugai Pharm. Co LTD (previously cited) is maintained for the reasons of record. Applicant does not provide any arguments to rebut the rejections, but instead has amended the claims to limit the mechanism of injury to the endothelial cells. Applicant's amendments have been carefully considered but are not deemed persuasive to overcome the rejection of record. JP 02 096535 teaches that the administration of epo to subjects that have been treated with carcinogenic substance or chemotherapeutics (see abstract). It is well known and established in the art (as evidenced by de Vos *et al* (Cancer Treat Rev. 2004 Oct;30(6):495-513) that the administration of chemotherapeutics to subjects cause vascular cytotoxicity/damage which include symptoms such as myocardial ischemia (a form of heart disease), vasculitis/inflammation of the blood vessel (see page 498), and in some cases physical disruption, such as cellular detachment (see page 500). Because the specification does not specifically define or limit the scope of the term "mechanical" damage or the types of heart disease encompassed, for the purposes of this rejection, the terms have been interpreted as any means of physical

damage/ disruption and any type of heart related ailment, respectively. Thus it is clear that the administration of a chemotherapeutic regimen as taught by the JP 02 096535 abstract caused endothelial damage mediated by mechanical damage, inflammation, and heart disease and therefore, the administration of epo to this population would also inherently treat endothelial injury as claimed. Moreover, because the mechanism of action is not patentable subject matter and because it appears that the method steps and product administered are identical, in the absence of evidence to the contrary and because the office does not have the facilities to determine otherwise, the method taught by the JP 02 096535 abstract would also treat endothelial cell injury as claimed. In the absence of evidence to the contrary, the method of Silvestris *et al* would also inherently reduce the suppression of endothelial cells growth and increase the number of endothelial cells growth as claimed.

With regard to claim 33, JP 02 096535 abstract teaches the administration of 500-100000 units/day, however upon examination of the translated document (see exhibit A, page 18), epo was administered at a dose of 170 units/kg. Therefore, the rejection of the claims under 35 USC 102(b) as being anticipated by JP 02 096535 is maintained for the reasons of record.

Claim Rejections Maintained - 35 USC § 102

7. The rejection of claims 16,31-33 and now newly rejected claims 17, and 19-20 under 35 USC § 102 as being anticipated by Bukowski *et al* (Blood 1994;84(10 Supp. 1):129A, IDS #3 9/02/2003) is maintained for the reasons of record. Applicant does not

provide any arguments to rebut the rejections, but instead has amended the claims to limit the mechanism of injury to the endothelial cells. Applicant's amendments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Bukowski *et al* teach the administration of epo to subjects that have undergone treatment with chemotherapeutic regimens (see abstract). It is well known and established in the art (as evidenced by de Vos *et al* (Cancer Treat Rev. 2004 Oct;30(6):495-513) that the administration of chemotherapeutics to subjects cause vascular cytotoxicity/damage which include symptoms such as myocardial ischemia (a form of heart disease), vasculitis/inflammation of the blood vessel (see page 498), and in some cases physical disruption, such as cellular detachment (see page 500). Because the specification does not specifically define or limit the scope of the term "mechanical" damage or the types of heart disease encompassed, for the purposes of this rejection, the terms have been interpreted as any means of physical damage/ disruption and any type of heart related ailment, respectively. Thus it is clear that the administration of a chemotherapeutic regimen as taught by the Bukowski *et al* caused endothelial damage mediated by mechanical damage, inflammation, and heart disease and therefore, the administration of epo to this population would also inherently treat endothelial injury as claimed. Moreover, because the mechanism of action is not patentable subject matter and because it appears that the method steps and product administered are identical, in the absence of evidence to the contrary and because the office does not have the facilities to determine otherwise, the method taught by the Bukowski *et al* would also treat endothelial cell injury as claimed. In the absence of

evidence to the contrary, the method of Silvestris *et al* would also inherently reduce the suppression of endothelial cells growth and increase the number of endothelial cells growth as claimed.

Therefore, the rejection of the claims under 35 USC 102(b) as being anticipated by Bukowski *et al* is maintained for the reasons of record.

NEW ARGUMENTS

Claim Rejections - 35 USC § 103

8. Claims 16-17,19-20,22,31-33, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Silvestris *et al* (Ann Hematol. 1995 Jun; 70(6):313-318) or Bukowski *et al* (Blood 1994;84(10 Supp. 1):129A, IDS #3 9/02/2003) in view of JP 02 096535 to Chugai Pharm. Co LTD.

a. The teachings of Silvestris *et al* (Ann Hematol. 1995 Jun; 70(6):313-318) as further evidenced by de Vos *et al* (Cancer Treat Rev. 2004 Oct;30(6):495-513) are set forth above and in previous office actions (see action mailed 7/02/2003) as they apply to claims 16-17,19-20, and 31-33.

b. The teachings of Bukowski *et al* (Blood 1994;84(10 Supp. 1):129A, IDS #3 9/02/2003) as further evidenced by de Vos *et al* (Cancer Treat Rev. 2004 Oct;30(6):495-513) are set forth above and in previous office actions (see action mailed 2/6/2004) as they apply to claims 16-17,19-20, and 31-33.

c. Both Silvestris *et al* and Bukowski *et al* do not specifically teach the administration of epo intravenously (claim 22 and 40).

d. JP 02 096535 to Chugai Pharm. Co LTD teach the administration of epo intravenously to subjects that have been treated with chemotherapeutics (see abstract).

It would have been *prima facie* obvious to one of skill in the art at the time the invention was made to modify the methods of any one of Silvestris *et al* or Bukowski *et al* so as to include the intravenous administration of epo to subjects that have been treated with chemotherapeutics for the purposes of treating endothelial injury. One would have been motivated to do so because the administration of epo intravenously to subjects was well known and would have provided one of skill in the art with a reasonable expectation of success. Further it would have been *prima facie* obvious to do so because both Silvestris *et al* and Bukowski *et al* taught the administration of epo subcutaneously to treat the same population of subjects and found success in doing so.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chritopher Yaen
Art Unit1642
December 22, 2004